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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,216	09/19/2003	Shaker A. Mousa	2747/1021	7027

7590 06/27/2005

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EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,216	MOUSA, SHAKER A.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) *6-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 43-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/13/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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Applicant's election with traverse of claims 1-5 and 43-54 of Group I in the reply filed on 4/27/2005 is acknowledged. The applicant failed to file the arguments in support of the traversal.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-42 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected subject matter.

Claims 1-5 and 43-54 are currently at issue in this application. An action on the merits of claims 1-5 and 43-54 is contained herein below.

35 U.S.C. 112, second paragraph rejection

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 and 43-54 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) In all occurrences of the presented claims, in the absence of the identity of "constituents" of heparin fraction, render the claims indefinite wherein applicant fails to articulate the identity, requisite to identifying the constituents of the heparin fraction.

(B) The terms "derivative" and "analogs" are relative terms, which render the claims 43 and 54 indefinite. In the absence of the specific derivatizations to the compound or analogs claimed core or distinct language to describe the structural modifications or the

chemical names of derivatized compounds or analogs claimed, the identity of said derivatives or analogs would be difficult to describe and the metes and bounds of said derivative or analog applicants regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claim.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons set forth supra.

35 U.S.C. 103(a) rejection

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 and 43-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mascellani et al. (Mascellani) (U.S. Patent 4,973,580) in view of Cohen et al. (Cohen) (U.S. Patent 5,908,837).

The applicants' claims are directed toward a heparin fraction or a composition thereof consisting of constituents having molecular weight between 2,000-4,000 daltons, wherein from about 1%- 100% of hydroxyl residues of the constituents are oxidized (claim 1) and from 0%-40% of heparin, low molecular weight heparin, chondroitin

sulfates, dermatan sulfates, heparin sulfates, heparin derivatives, or combinations thereof (claim 43).

Dependent claim limitations include 25%-100% oxidized hydroxyl residues (claims 2-4 and 44-46) and a sulfate to carboxylate ratio between 2:1 to 5:1 (claims 5 and 47); pharmaceutical acceptable carrier, excipient, or stabilizer (claim 48); a non-heparin anticoagulant (claims 49 and 50); non-heparin angiogenic inhibitor (claims 51 and 52); and a cytotoxic or chemotherapeutic agent (claims 53 and 54).

Mascellani discloses the depolymerized or oxidized heparins, heparin sulfate, dermatan sulfates and chondroitin sulfates (abstract). Mascellani discloses the oxidizing process of heparin with periodate to produce a reduced molecular weight product and a pharmaceutical composition thereof having a high antithrombotic activity, poor or no anticoagulant activity, a high fibrinolytic activity and an anti-inflammatory activity with a good bioavailabilty (col. 1, lines 15-25). Mascellani is silent in disclosing the oxidized percent range of the oxidized hydroxyl groups by the said process. Mascellani discloses the said heparin with a low molecular weight ranging between 2000-7000 (col. 4, lines 55-60). Mascellani also discloses the sulfate to carboxylate ratio between >2: 1 (col. 6, Table 1). Mascellani discloses that the oxidation process does not change the sulfate content of heparin, which is important for the biological activity (col. 4, lines 35-40). Mascellani differs from the applicant's invention that Mascellani does not provide an explicit example of a composition containing a heparin fraction in combination with a non-heparin agent or drug.

Cohen teaches the use of low molecular weight heparins in a pharmaceutical composition in combination with a non-heparin angiogenesis inhibitor (col.3, lines 50-60). Cohen discloses periodate oxidized heparins having a low molecular weight between 3000-6000, a pharmaceutical composition containing a pharmaceutical carrier (col. 4, lines 10-45). Cohen also discloses that the combination of the heparin and a non-heparin agent is more effective in the inhibition of angiogenesis (col. 3, lines 57-58). Therefore applicant's use of a non-heparin anticoagulant or a cytotoxic or chemotherapeutic agent in combination with the low molecular weight oxidized heparin fraction are obvious over the prior art.

It would have been obvious to person having ordinary skill in the art at the time the invention was made, to select heparin fraction or a composition thereof consisting of constituents having molecular weight between 2,000-4,000 daltons in combination with a non-heparin agent or drug, from among those taught by Mascellani and Cohen, because Mascellani discloses oxidized heparin with a low molecular weight ranging between 2000-7000 and Cohen teaches the use of low molecular weight heparins in a pharmaceutical composition in combination with a non-heparin angiogenesis inhibitor. Mascellani the motivation to use oxidized low molecular weight heparin fraction and a pharmaceutical composition thereof due to their high antithrombotic activity, poor or no anticoagulant activity, a high fibrinolytic activity and an anti-inflammatory activity with a good bioavailabilty (col. 1, lines 15-25).

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Supervisory Patent Examiner, Art Unit 1623 can be reached at 571-272-0661. The official fax phone numbers for the organization where this application or proceeding is assigned is (703) 308-4556 or 308-4242.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Devesh Khare, Ph.D.,J.D.
Art Unit 1623
June 20,2005